

REMARKS UNDER 37 CFR § 1.111

Formal Matters

Claims 23-28, 30-31 and 33-38 are pending after entry of the amendments set forth herein.

Claims 23-32 and 35 were examined. Claims 23-32 and 35 were rejected. No claims were allowed.

Claims 23, 26-28, 30 and 31 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to the claims is found in claim 32, as originally filed. Accordingly, no new matter is added.

Claims 29 and 32 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

PTO 1449 form

Applicants acknowledge receipt of an Examiner initialed PTO 1449 form submitted with the Information Disclosure Statement filed in this application on April 17, 2001, thereby indicating that the references cited therein have been reviewed and made of record.

Withdrawn claims

Claims 33-34 and 36-38 have been withdrawn by the Examiner.

In view of the amendments and remarks made herein, the Applicants earnestly request allowance of generic claim 23 and rejoinder of claims 33-34 and 36-38.

Priority

The cross-referencing paragraph has been objected to.

The Applicants have inserted the filing date of the parent application into this paragraph, and, as such, this objection has been adequately addressed.

Accordingly, this objection may be withdrawn.

Specification

The abstract is objected to for being over 150 words in length.

The abstract have been amended to remove a sentence. The length of the amended abstract is 145 words.

Accordingly, this rejection may be withdrawn.

The specification is objected to for reciting an “agonist” rather than “antagonist” in the context of atopic dermatitis.

The word “antagonist” is no longer present in the pending claims, and, as such, this objection is moot with respect to the pending claims. However, the word “agonist” at page 8, line 21, was an obvious error, and, accordingly, the specification has been amended to replace the word “agonist” with the word “antagonist”.

The Applicants respectfully submit that a skilled person would recognize that the word “agonist” was an obvious error because of the context of the application. For example, CCR antagonists “block CCR4 biological activity” (see page 9, lines 14-15) and “will cause a decrease in the T cell adhesion to the appropriate endothelial cell molecule” (see page 11, lines 11-12). Furthermore, the paragraph starting on page 8 line 22 discusses blocking CCR4 activity to inhibit accumulation of memory T cells to influence immune responsiveness. Since it is desirable to “decrease the number of systemic memory T-cells at the sites of inflammation” in order to treat atopic dermatitis (see the paragraph starting on page 8 line 15, particularly the last line), a skilled person would recognize that CCR antagonists may be used to treat diseases such as atopic dermatitis.

Accordingly, the Applicants respectfully submit that this error is an obvious error and respectfully request entry of this amendment.

The Applicants submit that this objection has been adequately addressed. Withdrawal of this rejection is respectfully requested.

Claim rejections under 35 U.S.C. §112, first paragraph (new matter)

Claim 35 is rejected under 35 U.S.C. §112, first paragraph, as containing new matter. The Applicants respectfully traverse this rejection.

The word “antagonist” is no longer present in the pending claims, and, as such, this objection is moot. Even if this rejection is not moot, the claim finds full support in the specification since, as discussed in the previous paragraph, a skilled person would clearly recognize from the specification that CCR antagonists, in particular antibodies, may be used to treat diseases such as atopic dermatitis.

The Applicants submit that this rejection has been adequately addressed. Withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph (written description)

Claims 23-31 and 35 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonable convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Without wishing to acquiesce to the correctness of this rejection and solely to expedite prosecution, the subject matter of claim 32, reciting an anti-CCR4 antibody, has been incorporated into claim 23. Since claim 32 was not included in this rejection and its subject matter is now included in claim 23, this rejection is believed to be moot.

In view of the foregoing discussion, withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph (enablement)

Claims 23-31 and 35 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Without wishing to acquiesce to the correctness of this rejection and solely to expedite prosecution, the subject matter of claim 32, reciting an anti-CCR4 antibody, has been incorporated into claim 23. Since claim 32 was not included in this rejection and its subject matter is now included in claim 23, this rejection is believed to be moot.

In view of the foregoing discussion, withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §102 - Barrett

Claims 23-25, 27-30 and 35 are rejected under 35 U.S.C. §102(b) as being anticipated by Barrett (USPN 5,643,873). The Applicants respectfully traverse this rejection.

Without acquiescing to the correctness of this rejection, claim 23 has been amended to incorporate the subject matter of claim 32, now cancelled: an anti-CCR4 antibody.

Since Barrett fails to disclose an anti-CCR4 antibody, it cannot anticipate the claims.

In view of the foregoing discussion, withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §102 – Li

Claims 23-25, 28-30 and 35 are rejected under 35 U.S.C. §102(e) as being anticipated by Li (USPA 2002/0098545). The Applicants respectfully traverse this rejection.

Without acquiescing to the correctness of this rejection, claim 23 has been amended to incorporate the subject matter of claim 32, now cancelled: an anti-CCR4 antibody.

Since Li fails to disclose an anti-CCR4 antibody, it cannot anticipate the claims.

In view of the foregoing discussion, withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §102 – Wells

Claims 23-25, 28 and 35 are rejected under 35 U.S.C. §102(e) as being anticipated by Wells (USPN 6,150,132). The Applicants respectfully traverse this rejection.

Without acquiescing to the correctness of this rejection, claim 23 has been amended to incorporate the subject matter of claim 32, now cancelled: an anti-CCR4 antibody.

As such, claim 23 is directed to a method of inhibiting the trafficking of systemic memory T cells to a site of inflammation in a mammalian host by administering an anti-CCR4 antibody.

Since Wells fails to disclose a method of inhibiting the trafficking of systemic memory T cells to a site of inflammation in a mammalian host by administering anti-CCR4 antibody, it cannot anticipate the claims.

In view of the foregoing discussion, withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §103 – Wells in view of Heath

Claims 23-30, 32 and 35 are rejected under 35 U.S.C. §103(a) as being unpatentable over Wells in view of Heath (J. Clin. Invest. 1997 99:178-184). Specifically, the Office Action asserts that the methods of identifying a CCR4 antagonist of Wells, in combination with Heath's suggestion to use monoclonal antibodies as chemokine receptor antagonists, renders the subject matters of the instant claims obvious. The Applicants respectfully traverse this rejection.

With regard to obviousness, the M.P.E.P. teaches at §1242 that:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, whether in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Thus, in order for a proper *prima facie* case to be established with a combination of references, all the elements of the claimed invention must be suggested in the references, and the invention must be suggested with a reasonable expectation of success.

The Applicants respectfully submit that Wells and Heath fail to teach an element of the rejected claims, namely a *systemic memory T-cell*. Furthermore, neither Wells nor Heath provide any indication that CCR4 (in view of the multitude of other chemokine receptors) would be a chemokine receptor useful in the claimed methods, and, as such, a skilled person would have no reasonable expectation of success in combining Wells and Heath to provide the claimed invention. Finally, Heath's negative statements regarding the function of CCR4 teach away from the claimed invention. The Applicants' reasoning is set forth below.

The rejected claims are directed to methods involving, *inter alia*, inhibiting trafficking of systemic memory T cells using an anti-CCR4 antibody.

Wells provides the sequence of CCR4, but fails to teach or in any way suggest methods of inhibiting trafficking systemic memory T cells using anti-CCR4 antibodies.

Heath, on the other hand, provides a method in which *eosinophil* chemotaxis is modulated using an anti-CCR3 antibody, and, according to the Office Action, generally suggests that chemokine receptor antagonists are effective inhibitors of leukocyte recruitment.

Firstly, neither Wells nor Heath mention systemic memory T-cells at any point. Accordingly, Wells and Heath, separately or in combination, fail to teach an element of the claimed invention, i.e., systemic memory T-cells.

On the basis of the foregoing, this rejection may be withdrawn without any further discussion.

Should the Examiner try to assert that the combination of Wells and Heath in some way does teach a method involving systemic memory T-cells, the Applicants respectfully submit that Wells and Heath cannot be combined to provide the claimed invention with any reasonable expectation of success. In other words, the Applicants respectfully submit that Heath's reported success in altering chemotaxis in eosinophils using an anti-CCR3 antibody would not automatically predict success of a method of altering chemotaxis of systemic memory T-cells using an anti-CCR4 antibody.

Heath teaches methods of altering chemotaxis of eosinophils. Eosinophils are not systemic memory T-cells (or even T-cells for that matter), and the Office has presented no reason why a method that works for eosinophils would work with a reasonable expectation of success in systemic memory T-cells. In fact, in view of comments made by Heath (see Heath's entire disclosure, and in particular the first sentence of the third paragraph of the introduction: "Because of the complicated pattern of receptor binding and signaling by the chemokines, it has been difficult to determine the significance of a particular receptor on a given leukocyte type") a skilled person would have no idea which receptor to block in order to effect chemotaxis of systemic memory T-cells. In other words, in view of the teachings of Wells and Heath (in particular the comments made by Heath) a skilled person would not know beforehand which chemokine receptor (e.g., CXCR1, CXCR2, CCR1, CCR2, CCR3, CCR4, or CCR5, or any other chemokine receptor not specifically listed by Wells or Heath) would be a successful target for altering chemotaxis of systemic memory T-cells. In actual fact, prior to filing of this patent application, it was not even known that systemic memory T-cells actually expressed CCR4. Why would a skilled person think that CCR4 is the chemokine receptor responsible for chemotaxis of systemic memory T-cells? The Applicants respectfully submit that the answer to this question is not set forth in

Wells or Heath, or in the Office Action, and it was not until the Applicants made this discovery that the answer became known.

Furthermore, at several positions Heath indicates that CCR4 has no role in chemotaxis of eosinophils. For example:

On page 181 in the first paragraph of the discussion, Heath states the following:

“These results establish that CCR3 is indeed the principal receptor for eosinophil responses to CC chemokines, and questions the essential role for CCR1, CCR2, CCR4 or CCR5.”

(emphasis added)

On page 181 in the second paragraph of the discussion, Heath states the following:

“...our results show that a MIP-1 α receptor [Wells asserts that CCR4 is the receptor for MIP1 α and RANTES. See, e.g., Wells column 1, title, and the last paragraph of column 1]. contributes little to the functional responses of eosinophils to the major eosinophilic chemoattractants: RANTES, MCP-3 or MCP-4”.

(emphasis and bracketed material added)

And on page 181 in the second paragraph of the discussion, Heath also states the following:

“...if other CC chemokine receptors are present [e.g., CC chemokine receptors other than CCR3, e.g., CCR4], they have a minor functional significance”

(emphasis and bracketed material added)

In other words, Heath teaches that CCR4 has no role in eosinophil chemotaxis. The Applicants respectfully submit that Heath’s comments on the function of CCR4 would, in fact, lead a skilled person away from any conclusion that CCR4 is the chemokine receptor responsible for chemotaxis of systemic memory T-cells. Set forth another way, Heath states that CCR4 is functionally insignificant in relation to CCR3 in eosinophils. Since there would be no reason for this not to be true in systemic memory T-cells, a skilled person would be more likely to think that CCR3, not CCR4, is the chemotaxis receptor in systemic memory T-cells. This conclusion is supported by fact that Heath found CCR3 in some T-cell

clones (see the second sentence of the second paragraph of Heath's discussion). In view of Heath's teachings, therefore, a skilled person would more likely suspect CCR3, not CCR4 as being the primary receptor for systemic memory T-cells.

Accordingly, even if the combination of Wells and Heath did teach systemic memory T-cells, the subject matter of the rejected claims could not be practiced with any reasonable expectation of success because there is no suggestion that CCR4 is the dominant receptor for systemic memory T-cells. To the contrary, Heath teaches that CCR3, and not CCR4, is the dominant receptor for systemic memory T-cells. Since the subject matter of the rejected claims cannot be practiced with any reasonable expectation of success, this rejection may be withdrawn.

Rejection under 35 U.S.C. §103 – Wells in view of Heath and Bendig

Claim 31 is rejected under 35 U.S.C. §103(a) as being unpatentable over Wells in view of Heath and Bendig (Methods: A Companion to Meth. Enzymol. 1995 8:83-93). Specifically, the Office Action asserts that the methods of identifying a CCR4 antagonist of Wells, in combination with Heath's suggestion to use monoclonal antibodies as chemokine receptor antagonists and Bendig's humanized monoclonal antibodies, renders the subject matters of the instant claims obvious. The Applicants respectfully traverse this rejection.

As established above, Wells and Heath are deficient in that they fail to teach systemic memory T-cells.

Bendig's humanized monoclonal antibodies fail to meet Wells and Heath's deficiencies, and, as such, an element of claim 31, i.e., systemic memory T-cells, is not taught in this rejection.

Furthermore, as established above, Wells and Heath cannot be combined to produce the claimed invention with any expectation of success. Bendig, in addition to failing to provide an element of the claims, also fails to provide an expectation of success.

In view of the foregoing, this rejection may be withdrawn.

Rejection for Obviousness-Type Double Patenting

Claims 23-32 and 35 stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-15 of US patent 6,245,332.

The Applicants categorically disagree with this rejection.

However, solely to expedite prosecution, the Applicants provide herewith a terminal disclaimer over US patent 6,245,332.

The Applicants note that the filing of a terminal disclaimer to obviate a rejection based on nonstatutory double patenting is not an admission of the propriety of the rejection.¹ As such, while the Applicants firmly believe that this rejection fails to meet the requirements for Obviousness-Type Double Patenting set forth in MPEP § 804, a terminal disclaimer is filed to obviate the rejection.

Withdrawal of this rejection is respectfully requested.

¹ *Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 20 USPQ2d 1392 (Fed. Cir. 1991). The court indicated that the "filing of a terminal disclaimer simply serves the statutory function of removing the rejection of double patenting, and raises neither a presumption nor estoppel on the merits of the rejection."

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-110CON.

Respectfully submitted,
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